

For older adults (age>65), what is the effect of weight loss versus weight maintenance on health outcomes (cardiovascular disease, Type 2 diabetes, cancer, and mortality)?

Conclusion

Weight loss in older adults has been associated with an increased risk of mortality, but because most studies have not differentiated between intentional vs. unintentional weight loss, recommending intentional weight loss has not been possible. Recently, however, moderate evidence of a reduced risk of mortality with intentional weight loss in older persons has been published. Intentional weight loss among overweight and obese older adults, therefore, is recommended. In addition, with regard to morbidity, moderate evidence suggests that intentional weight loss in older adults has been associated with reduced development of type 2 diabetes and improved cardiovascular risk factors. There are insufficient data on cancer to come to a conclusion. Weight gain produces increased risk for several health outcomes.

Grade: Moderate

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades [click here](#).

Evidence Summary Overview

The risks and benefits of weight loss in older adults have been widely debated. While it has been clearly reported that weight loss improves risk factors for diabetes and cardiovascular disease (CVD) (Pi-Sunyer, 2007; Villareal, 2006; Whelton, 1998), some studies have showed that weight loss increases mortality (Knudtson, 2005; Sorenson, 2003; Yaari, 1998). However, it is not clear in these studies whether the weight loss was intentional or unintentional.

Thirty-five cohort studies, two longitudinal observational studies, one structural equation model and one randomized controlled trial (RCT) were reviewed, dating from 1995 to the present. There was strong unanimity that, in elderly persons followed for two to 23 years, a baseline body mass index (BMI) below normal ($18.5\text{--}25\text{kg/m}^2$) was associated with a higher risk of mortality whereas a BMI above normal ($>25\text{kg/m}^2$) was associated with a lower risk. The mortality curve in relation to baseline BMI was U-shaped, with minimal mortality risk occurring over a wide range (BMI of 25 to 34kg/m^2). In a modeling report by Yang et al, (2008), the highest life expectancy was in subjects with a BMI range of 18.5 to 25kg/m^2 .

Weight loss in elderly persons was associated with a higher mortality, but no data were available about the intentionality of the weight loss except for one study by Locher et al, (2007) in a three-year follow-up of subjects with a mean age of 73 years, who found that non-intentional weight loss was associated with higher mortality whereas intentional weight loss was not. A recent RCT (Shea, 2010) assessed the influence of weight loss or exercise in overweight and obese older adults with knee osteoarthritis. After an average of eight years of follow-up, the mortality rate was significantly lower for those randomized to the weight loss intervention, who initially lost 4.8kg. Intentional weight loss therefore did not lead to increased total mortality but actually reduced it. In addition, interventional studies have shown that this intentional weight loss in older persons is not associated with greater adverse events (Diabetes Prevention Program Research Group, 2002; Pi-Sunyer, 2007; Whelton, 1998).

With regard to the risk of developing diabetes, CVD or cancer with weight loss, one study has reported that

both type 2 diabetes (T2D) and CVD risk factors can be improved with weight loss in older Americans. Another study has shown that in people with T2D, intentional weight loss improves glycemia and CVD risk factors (Pi-Sunyer, 2007) and Whelton et al, (1998) have reported that intentional weight loss lowers blood pressure (BP). The SOS study (Sjostrom, 2007), while a bariatric surgery study, has shown that intentional weight loss with bariatric surgery greatly lowers the risk of morbidity for T2D, CVD, as well as mortality for CVD and cancer, in more elderly as well as younger subjects.

Weight gain was associated with either the same or higher mortality than in weight maintenance.

Evidence Summary Paragraphs

Randomized Controlled Trials (1)

Shea et al, 2010 (positive quality) conducted a RCT in the United States to assess the influence of weight loss on total mortality in overweight and obese older adults. Subjects were randomized to one of four treatment groups: Dietary weight loss, exercise, dietary weight loss plus exercise or a healthy lifestyle control group. The intervention was 18 months long. Body weight and height were measured and used to determine BMI and weight status and mortality was determined using the Social Security Index and the National Death Index. The final sample included 319 adults (72% female; mean age=96 years; mean BMI=34kg/m²). The mortality rate for those randomized to the 18-month weight loss intervention (mean weight loss= -4.8 kg) was lower than that for those not randomized to the weight loss intervention (mean weight loss= -1.4kg) (HR 0.5, 95% CI 0.3-1.0). Results did not change when adjusted for age, gender, baseline weight status or magnitude of weight loss. The authors concluded that intentional weight loss was not associated with increased mortality and may reduce mortality risk among overweight and obese older adults.

Cohort Studies (35)

Allison DB et al, 1997 (neutral quality) used prospective cohort data from the Longitudinal Study of Aging cohort study conducted in the United States to assess the relationship between BMI and mortality. Body mass index was based on self-reported height and weight, while mortality was obtained by record matching to the National Death Index. Of 7,397 men and women aged 70 and older in the original cohort in 1984, 7,260 were followed through 1990. The relationship between BMI and mortality was U-shaped for both men and women; the minimum mortality occurred at a BMI of 31.7kg/m² for women and 28.8kg/m² for men.

Amador LF et al, 2006 (positive quality) analyzed data from a prospective cohort study conducted in the United States to examine the association between two-year weight change and mortality in older Mexican Americans, using data from the Hispanic Established Population for the Epidemiological Study of the Elderly (ESPESE). Weight change was based on measurements made at baseline and at the two-year follow-up and participants were followed for mortality over the next five years. Of 3,050 subjects aged 65 and older originally in the cohort at baseline, 1,749 were included in the analysis. Over two years, 396 (22.6%) had lost 5% or more weight (and 28% had died during follow-up), 984 (56.3%) were weight stable (19.7% had died during follow-up) and 369 (21.1%) had gained 5% or more weight (15.2% had died during follow-up). After controlling for confounding variables, compared to the weight stable group, the hazard ratio (HR) of death for the group that lost 5% or more of their weight was 1.32 (95% CI: 1.04-1.67) and for the group that gained 5% or more of their weight was 0.77 (95% CI: 0.57-1.04).

Arnold AM et al, 2009 (positive quality) conducted a prospective cohort study to determine the associations between weight, physical functioning and mortality in older adults in the United States. Subjects were from the Cardiovascular Health Study. Weight was measured annually in a clinic between 1992 and 1999. Subjects were then followed until 2006 with regular assessments of activities of daily living, mobility and mortality. The final sample included 3,278 adults (39% men; mean age=80 years). Higher weight, increased weight variability and weight cycling were all associated with increased risk of difficulties with activities of daily living (1.28 (95% CI 1.12, 1.47) and mobility limitations (1.25 (95% CI 1.09, 1.42). Weight loss was associated with increased mortality (1.58 (95% CI 1.33, 1.88), as was weight cycling (1.66 (95% CI 1.38, 2.00). The authors concluded that variation in weight is an important indicator of future physical limitations

and mortality in older adults and fluctuations in weight should be monitored.

Corrada MM et al, 2006 (neutral quality) used data from the population-based Leisure World Cohort Study conducted in the United States to explore the associations between weight change and all-cause mortality in the elderly. All 13,978 residents of the Leisure World Laguna Hills retirement community returned mailed questionnaires in 1981, 1982, 1983 and 1985; data from 13,451 residents (mean age 73 years) was included in the analysis. Residents reported weight and height at age 21 and weight change was calculated as percent change in weight from age 21 to study entry. All-cause mortality was confirmed by periodic resurveys, reviews of local hospital discharge records, and determination of vital status through searches of national and commercial death indexes. During 23 years of follow-up (1981-2004), 11,203 residents died. Relative to normal weight, being underweight (RR=1.51, 95% CI: 1.38-1.65) or obese (RR=1.25, 95% CI: 1.13-1.38) at study entry was associated with increased mortality. In addition, residents who were either overweight or obese at age 21 also had increased mortality (RR=1.17, 95% CI: 1.09-1.25); obesity was significantly associated with increased mortality only among persons under age 75 years and among never or past smokers.

de Groot CP et al, 2002 (neutral quality) analyzed prospective cohort data from Europe to assess longitudinal changes in height, body weight and circumferences in elderly European subjects from the SENECA study. Baseline measurements were taken in 1988 and 1989 and repeated in 1993 and 1999. Of 2,040 subjects originally in the cohort, baseline anthropometric data was collected from 1,958 examinees (927 men and 929 women, aged 81-86 years) and measurements were repeated in 662 subjects (292 men and 370 women). On average, stature decreased by 1.5-2 cm and waist circumference increased by 3-4cm over the 10-year follow-up; 13% of men and women had gained at least 5kg of body weight, while 23% of men and 27% of women had lost at least 5kg of body weight. Weight loss during the first four years of follow-up was associated with higher mortality rates in men (crude RR=2.2, P<0.0001).

Dey DK et al, 2001 (positive quality) utilized longitudinal cohort data from Sweden to examine the relationship between BMI, weight change and mortality in the elderly. Three birth cohorts (born in 1901 and 1902, 1906 and 1907, and 1911 and 1912) were followed over a 15-year period, and BMI was based on measured height and weight. Of 2,628 elderly men and women originally in the three cohorts (1,148 born in 1901 and 1902, 1,281 born in 1906 and 1907, and 806 born in 1911 and 1912), complete data were available for 2,593 subjects (aged 70 years and older). The relative risks for 15-year mortality were highest in the lowest BMI quintiles of males (RR=1.20, 95% CI: 0.96-1.51) and females (RR=1.49, 95% CI: 1.14-1.96). After exclusion of the first five years of death, no excess risks were found in males for following five-year and 10-year mortality across the quintiles, but in females, a U-shaped relation was observed. BMI ranges with lowest 15-year mortality were 27-29 kg/m² in non-smoking males and 25-27kg/m² in non-smoking females. In addition, a weight loss of >10% between ages 70 and 75 resulted in a significantly higher risk for subsequent five-year and 10-year mortality in both sexes relative to those with stable weights.

Diehr P et al, 1998 (neutral quality) conducted a prospective cohort study in the United States to assess the relationship between BMI and five-year mortality in older adults. Subjects were from the Cardiovascular Health Study. Body mass index was determined at baseline using measured height and weight and follow-up all cause mortality was determined five years later. The final sample included 4,317 adults (2,410 women, 1,907 men; mean age=73 years). There was an inverse association between BMI and mortality, such that those who weighed the least had the highest mortality rates (P<0.01). Subjects who lost ≥10% of their weight since age 50 had a higher mortality rate (16% for women, 30% for men); however, when this group was excluded from analyses, there was no longer a relationship between BMI and mortality. The authors concluded that overweight was not associated with increased mortality risk in this group, but that the risks associated with weight loss were of concern.

Diehr P et al, 2008 (neutral quality) used longitudinal cohort study data from the United States to determine whether weight categories predict subsequent mortality and morbidity in older adults, using 5,201 participants from the Cardiovascular Health Study and a supplemental cohort of 687 African Americans. A total of 5,888 participants were included in the analysis (mean age 75.7 years). Based on multistate life tables, the age- and sex-specific probabilities of transition from one health state to another and from one

weight category to another were estimated. Women who were healthy and at normal weight at age 65 years have a life expectancy of 22.1 years, with 9.6 of those years as overweight and obese and 5.3 of those years in fair or poor health. For both men and women, being underweight at age 65 years was associated with worse outcomes than being normal weight. In addition, being overweight or obese was rarely associated with worse outcomes than being normal weight and was sometimes associated with significantly better outcomes.

Dolan CM et al, 2007 (positive quality) conducted a prospective cohort study in the United States to examine the relationship between body size and mortality in women aged 65 years or older. Subjects were from the Study of Osteoporotic Fractures. At baseline, body composition was measured via bioelectrical impedance and BMI was determined using measured height and weight. Average follow-up occurred eight years later, when mortality was assessed. The final sample included 8,029 women (mean age=72 years), with 945 deaths occurring by the eight year follow-up. Mortality rates were lowest for women in the middle distribution of each measure of body size. Lowest mortality rates were seen in the BMI range from 24.6 to 29.8 kg/m² and all body measures had a U-shaped relation with mortality ($P<0.05$), such that increased mortality was associated with BMI above and below this range. The authors concluded that older women in the overweight BMI range had significantly lower mortality risk compared to women in the normal-weight, under-weight and obese ranges.

Ellekjaer H et al, 2001 (positive quality) conducted a prospective cohort study in Norway to examine the association between BMI and cerebrovascular and cardiovascular mortality in a population of healthy elderly. Height, weight and BMI were determined at baseline, and mean follow-up time was 7.7 years. The final sample included 3,121 men and 3,271 women 70 years and older. In women, a negative association between BMI and mortality from CVD death was found after age-adjustments ($P=0.03$) and no association was seen after adjusting for age by one year, systolic BP, BMI quartiles, current smoking ($P=0.16$). In men, no association between BMI and mortality from CHD was found after age-adjustments ($P=0.65$) or further adjustments ($P=0.71$). No association was found between BMI and mortality from CHD in men or in women with age or further adjustments. A negative association was found between increasing BMI and all-cause mortality in men and women in age-adjusted analyses (both $P<0.01$) but in multivariate analyses, the negative association was statistically significant only in women ($P<0.01$).

Grabowski DC et al, 2001 (neutral quality) used retrospective cohort study data from the United States to determine the excess mortality associated with obesity in older people, with and without adjustment for other risk factors associated with mortality and for demographic factors, based on participants in the Longitudinal Study of Aging. Baseline information, including self-reported height and weight, was collected in 1984, and survival was measured for eight years until December 1991 using the National Death Index. Of 7,527 participants in the original cohort, 7,459 subjects were included in the analysis (62% female, 38% male, mean age 76.8 years). During the follow-up period, death occurred in 38% of the cohort: 54% of those who were underweight (BMI $<19.4\text{kg/m}^2$), 33% of those who were obese (BMI $>28.5\text{kg/m}^2$) and 37% of normal-weight participants. Adjustment for confounding variables still demonstrated reduced mortality in obese older people (HR=0.86, 95% CI: 0.77-0.97) compared with normal-weight older people. In addition, after adjustment, underweight older people remained more likely to die (HR=1.46, 95% CI: 1.30-1.64) than normal-weight older people.

Graham JE et al, 2009 (positive quality) conducted a prospective cohort study in the United States to determine the ability of a widely used measure of frailty to predict 10-year mortality in a large population-based sample of Mexican American older adults. The study dataset covers the period from wave two (1995-1996) through wave five (1993-1994). Data were collected from in-person interviews and performance evaluations at each wave (approximately two-year intervals). Frailty was determined using a five-item scale based on weight loss, exhaustion, walking speed, grip strength, physical activity. The final sample included 1,996 adults (42% men; mean age=75 years; mean BMI=28kg/m²). In the fully adjusted model (controlling for sociodemographic, health-related factors and medical conditions), the pre-frail group had 1.25 times (95% CI: 1.07, 1.46) the odds of mortality relative to the non-frail group, and the group classified as frail at baseline had an increased odds of 1.81 (95% CI: 1.41, 2.31) of mortality. The authors concluded that frailty status is associated with increased 10-year mortality in older Mexican Americans.

Inoue K et al, 2006 (positive quality) analyzed prospective cohort data from Japan to assess the relationship between BMI and mortality rate in a sample population of Japanese seniors residing at home who had volunteered for an annual health check program. Body mass index was calculated from measured height and weight and the mortality register was followed for five years. Of 1,020 elderly residents aged 65 years or older, 371 participated in the health check program. At baseline, 54 subjects (14.6%) had BMI values in the low range ($<18.5\text{kg/m}^2$), 280 (75.5%) in the normal range ($18.5\text{-}25.0\text{kg/m}^2$) and 37 (10.0%) in the high range ($>25.0\text{kg/m}^2$); over the five-year follow-up period, 37 subjects had died. The mortality rate in the low BMI group was approximately twice that in the normal BMI group, and no deaths were observed in the high BMI group. In multivariate analyses, age and low BMI were associated with mortality.

Janssen I, 2007 (positive quality) conducted a prospective cohort study in the United States to examine the health risks associated with overweight and obesity in adults age 65 and older. Participants were from the Cardiovascular Health Study (CHS), a population-based longitudinal study of coronary heart disease (CHD) and stroke. Weight and height were measured at baseline. Mortality and myocardial infarction (MI) or stroke were ascertained for up to nine years, diabetes status was measured at baseline, three-year and seven-year follow-up examinations, and cancer status was measured at baseline, one-year, three-year and four-year follow-up examinations. The final sample included 4,968 subjects (44.6% men: 43% 65-70 years, 33% 71-76 years, 18% 77-82 years, and 7% >83 years). In the final adjusted model, the risk estimates for all-cause mortality were 11% lower in the overweight group and 17% lower in the obese group compared to the normal weight group ($P<0.05$). Compared with the normal weight group, the hazards ratio for MI, stroke and cancer were not different in the overweight group ($P>0.05$). The risk for developing diabetes was increased by 78% within the overweight group (vs. normal weight group, $P<0.01$). The authors concluded that a BMI in the overweight range was associated with some modest disease risks, but a slightly lower overall mortality rate.

Janssen I et al, 2005 (positive quality) used data from a longitudinal cohort study conducted in the United States to examine the effects of BMI and waist circumference (WC) on mortality risk in elderly men and women participating in the Cardiovascular Health Study. The baseline exam was conducted between June 1989 and June 1990, and BMI was calculated based on measured height and weight; WC was also measured. The cohort was followed annually for nine years after the baseline exam, and all-cause mortality was assessed through reviews of obituaries, medical records, death certificates and the US Center for Medicare and Medicaid Services health utilization database for hospital stays. A total of 5,200 participants over age 65 were included in the analysis (2,263 males and 2,937 females). When examined individually, BMI and WC were both negative predictors of mortality, however, when examined simultaneously, BMI was a negative predictor and WC was a positive predictor. After controlling for WC, mortality risk decreased 21% for every standard deviation (SD) increase in BMI, and after controlling for BMI, mortality risk increased 13% for every SD increase in WC.

Kalmijn S et al, 1999 (positive-quality) analyzed prospective cohort data from the United States to study the association between body weight and fat distribution with mortality in older male subjects from the Honolulu Heart Program. Body weight, height, body composition and waist-to-hip ratio (WHR) were measured during the study period; data were extracted from the 1991-1993 follow-up visits and included 4.5 years of follow-up. Of 4,676 male subjects in the cohort, 3,594 were included in the analysis (aged 71-93 years). During the follow-up period, 766 men (21%) had died. Higher BMI was associated with lower adjusted mortality risks (RR for the highest vs. lowest quintile-based category=0.5, 95%CI=0.4-0.6, P for trend <0.001). The relationship between WHR and mortality appeared to be U-shaped, but after adjustment for BMI, a higher WHR steadily increased the risk of dying (RR for the highest vs. lowest category=1.5, 95% CI: 1.1-2.0, P for trend=0.004). Especially in subjects with high BMI, there was a positive association between WHR and mortality.

Keller and Ostbye, 2005 (positive quality) used data from a cohort study conducted in Canada to investigate the predictive ability of the BMI categories identified in the WHO Weight Classification System and change in BMI on mortality in participants from the Canadian Study of Health and Aging. The final sample included 539 subjects (30.6% were aged 65-74 years, 55.8% were aged 75-84 years, and 13.5% were aged 85 years and older). Participants underwent a clinical examination (including body weight measurements) in 1991 and

1996, and mortality was determined via decedent questionnaires and death certificate information. A significant decrease in BMI predicted death (OR, 2.10; 95% CI: 1.17, 3.80); other factors predictive of death were age and cognitive impairment.

Knudtson et al, 2005 (positive quality) analyzed data from a cohort in the United States to investigate the relationship between weight loss in older adults and risk of death. Subjects were recruited in 1988 and 1990 and followed for 10 or more years. A medical examination and questionnaire were administered at baseline. Death was determined via follow-up telephone calls and review of vital statistics records. The final sample included 4,926 subjects. After controlling for age, medical and lifestyle factors, both men and women had higher mortality rates over a more than 10-year period for increasing categories of weight loss (HR 1.16, 95% CI 1.06, 1.27 for men; HR 1.23, 95% CI 1.13, 1.34 for women). The authors concluded that there was a strong association between weight loss and mortality, but that this weight loss was likely involuntary.

Kulminski AM et al, 2008 (neutral quality) used cohort data from the United States to investigate the association between BMI and long-term mortality in disabled and non-disabled older individuals using data from the 1994 National Long-Term Care Survey. Body mass index were based on self-reported height and weight; mortality was followed for nine years based on Medicare vital statistics files. Of 5,088 individuals over age 65 in the 1994 National Long-Term Care Survey, data for 4,791 individuals were included in the analysis. During the follow-up period, 2,956 individuals died. The relative risk of death as a function of BMI formed a non-symmetric U-shaped pattern, with larger risks associated with lower BMI ($<22.0 \text{ kg/m}^2$) and minimal risks for BMI $25.0\text{--}34.9 \text{ kg/m}^2$. Non-disabled individuals exhibited a similar U-shaped pattern but with lower risks associated with lower BMI. For disabled individuals, the mortality-risk pattern was higher for lower BMI ($<22.0 \text{ kg/m}^2$) and flat for higher BMI, thus exhibiting an inverse J shape.

Mazza A et al, 2007 (positive quality) analyzed prospective cohort data from Italy to investigate the role of BMI as a predictor of mortality in elderly subjects aged 65 years and older participating in the Cardiovascular Study in the Elderly (CASTEL). Body mass index was calculated based on measured height and weight from the initial screening, and participants received an annual follow-up for mortality for 12 years, which was determined from the Registry office and double-checked for causes of death by referring to hospitals, retirement homes or physicians' files. A total of 3,292 subjects were included in the analysis (1,281 males and 2,001 females, mean age 73.8 ± 5.3 years at baseline). BMI inversely predicted overall and cancer mortality in men only and there was no relationship between BMI and coronary or cerebrovascular mortality. The relationship between BMI and mortality remained significant only in men aged 76 years or less; overall mortality was 64.7% in the first BMI quintile, 54.9% in the second BMI quintile, 54.1% in the third BMI quintile, 53.3% in the fourth BMI quintile and 52.5% in the last BMI quintile.

Newman AB et al, 2001 (positive quality) conducted a longitudinal observational cohort study in the United States to identify health and behavior factors associated with changes in measured weight to explain the association between weight change and mortality in community-dwelling older adults participating in the Cardiovascular Health Study. Weight was measured at baseline and at the three-year follow-up visit and participants were followed for four years for mortality. Of the 5,888 adults aged 65 and older originally in the sample (5,201 from the Cardiovascular Health Study and 687 African Americans additionally recruited), 4,714 were included in the analysis. Weight changes occurred in 34.6% of women and 27.3% of men, with weight loss being more frequent than weight gain. While weight gain was not associated with increased risk of mortality, weight loss of 5% or more was associated with an increased risk of mortality that persisted after multivariate adjustment (HR=1.67, 95% CI: 1.29-2.15). Those with weight loss and with low baseline weight had the highest crude mortality rate, although the hazard ratio for weight loss was similar for all tertiles of baseline weight compared with those whose weight was stable.

Nguyen ND et al, 2007 (positive quality) analyzed data from a longitudinal cohort study conducted in Australia to assess the independent association between bone loss, weight loss and weight fluctuation in the prediction of all-cause mortality risk in elderly men and women participating in the Dubbo Osteoporosis Epidemiology Study. Bone density was measured by dual-energy x-ray absorptiometry (DEXA) at baseline and approximately every two years afterward, while all-cause mortality was recorded annually between 1989 and 2004. A total of 1,703 subjects were included in the analysis (1,059 women and 644 men, aged 60 and

older). In men, independent risk factors of all-cause mortality included a rate of bone density loss of at least 1% per year, a rate of weight loss of at least 1% per year and a weight fluctuation of at least 3%. In women, lower baseline bone density was also an independent risk factor of mortality in addition to the factors observed in men. However, in both sexes, baseline weight was not an independent and significant predictor of mortality risk.

Payette H et al, 1999 (positive quality) used prospective cohort study from Canada to evaluate the impact of nutritional risk factors on mortality in a frail elderly population receiving home help services. Height, weight and dietary intake were measured at baseline, and subjects were followed for mortality for three to five years. A total of 288 subjects were included in the analysis (207 women, 81 men, mean age 78.2 ± 7.6 years). During the follow-up period, 102 participants (35.4%) died; predictors included age, sex, BMI, weight loss and functional status. In multivariate analyses, weight loss at baseline was a significant predictor of mortality (RR=1.76, 95% CI: 1.15-2.71), as was male gender (RR=2.71, 95% CI: 1.73-4.24) and age at baseline (RR=1.40, 95% CI: 1.06-1.86).

Price GM et al, 2006 (positive quality) conducted a prospective cohort study in the United Kingdom to investigate the associations between BMI, waist circumference (WC), and waist-to-hip ratio (WHR) with mortality in adults ≥ 75 years of age. Subjects had anthropometric measures taken at a clinic visit, and average follow-up time was 5.9 years. The final sample included 14,833 adults (5,715 men, 9,118 women), of which 6,649 subjects died during the period until follow-up. Compared to the lowest BMI quintile (<23 in men, <22.3 in women), adjusted hazard ratios for mortality were less than one for all other BMI quintiles ($P=0.0003$ for men, $P=0.0001$ for women). Increased WHR was associated with increased hazard ratios in men ($P=0.008$) and women ($P=0.0002$). In men, BMI was not associated with circulatory mortality, but it was positively associated in women ($P=0.004$). Waist circumference was not associated total or circulatory mortality in men or women. The authors concluded that increased abdominal obesity (assessed via waist-to-hip) ratio was associated with increased mortality risk, while current BMI-based risk categories overestimate the risk of excess weight in older adults.

Reynolds MW et al, 1999 (positive quality) used prospective cohort data from the United States to evaluate the relationship between measured weight, weight change and six-year mortality risk using a sample of community-dwelling women aged 65 and older. Three home interviews were conducted annually from 1984 to 1986; height and demographic information was obtained during the baseline interview, while weight was measured at each interview. Of 806 women originally in the cohort, 648 were included in the analysis (mean age 73 ± 6.1 years). During the follow-up period, 106 women (16%) died; women with low baseline BMI ($<23 \text{ kg/m}^2$), regardless of weight change, and those who lost weight, regardless of baseline BMI, had increased mortality risk. In addition, women with average baseline BMI ($23\text{--}28 \text{ kg/m}^2$) and weight loss had a very high mortality risk (HR=3.84, 95% CI: 2.14-6.89). Women who weight cycled had increased mortality risk at both low and high baseline weights.

Rodriguez C et al, 2002 (positive quality) conducted a prospective cohort study in the United States to examine the relationship between BMI, height and ovarian cancer mortality in postmenopausal women. BMI at baseline was calculated based on self-reported height and weight and subjects were followed for 16 years, when mortality was determined using personal inquiries and the National Death Index. The final sample included 300,527 women, 1,511 of which died from ovarian cancer during the 16 year follow-up period. Ovarian cancer mortality rates were higher in overweight (1.16 (95% CI 1.04, 1.30) and obese (1.26 (95% CI 1.07, 1.48) women compared to normal weight women. This relationship was mediated by use of postmenopausal estrogens, as the increased risk of ovarian cancer among obese women was limited to those who never used postmenopausal estrogen (1.36 (95% CI 1.12, 1.66). Height was also related to ovarian cancer mortality, with the shortest women ($<152 \text{ cm}$) having the lowest risk of ovarian cancer (0.72 (95% CI 0.47, 1.10) compared to the tallest women ($>177 \text{ cm}$; 1.41 (95% CI 0.95, 2.09). The authors concluded that obesity and height were independently associated with risk of death from ovarian cancer.

Sorensen TI et al, 2005 (positive quality) analyzed data from a prospective cohort study conducted in Finland to examine the influence on mortality of intention to lose weight and subsequent weight changes in overweight older adults. Subjects were from The Finnish Twin Cohort, who were recruited in 1975 and

followed through 1999. Weight and BMI was determined using self-reported height and weight and mortality as determined using the Statistics Finland database. The final sample included 2,957 subjects (BMI >25kg/m²; 268 died during the follow-up period). Compared with the group not intending to lose and able to maintain stable weight, the hazard ratios in the group intending to lose weight were 0.84 (95% CI 0.49-1.48) for those with stable weight, 1.86 (95% CI 1.22-2.87) for those losing weight and 0.93 (95% CI 0.55-1.56) for those gaining weight. In the group not intending to lose weight, hazard ratios were 1.1 (95% CI 0.82-1.66) for those who did not lose weight and 1.57 (95% CI 1.08-2.30) for those gaining weight. The authors concluded that deliberate weight loss among older overweight individuals may be hazardous in the long term.

Sullivan DH et al, 2002 (neutral quality) used data from a prospective cohort study conducted in the United States (the Geriatric Anorexia Nutrition (GAIN) registry) to determine:

1. Which nutrition or health status indicators correlated with subsequent weight gain or appetite improvements
2. Whether a continued weight loss correlated with higher mortality. Nutritional, health status, and demographic data was obtained through nursing home charts or other means.

Each subject was followed for six months. The final sample included 894 subjects (mean age, 86±8 years) in 96 long-term care facilities distributed among eight states. Results showed that predictors of a 5% or greater weight gain within six months included BMI (adjusted OR, 0.89; 95% CI, 0.85 to 0.93), age (adjusted OR, 0.96; 95% CI, 0.94-0.98), feeding dependency (adjusted OR, 0.55; 95% CI, 0.34 to 0.89) and receiving appetite stimulants (adjusted OR, 1.70; 95% CI, 1.06 to 2.72). A weight loss during the six-month period was associated with nearly two-fold increase in the risk of death (adjusted RR: 1.95, 95% CI, 1.46 to 2.66).

Sullivan DH et al, 2004 (neutral quality) used data from a prospective cohort study conducted in the United States to evaluate the prognostic significance of weight change in frail elderly patients in a Department of Veterans Affairs hospital. At admission and discharge, subjects completed a standardized diagnostic evaluation, and weights were recorded before admission, during the current hospitalization, and after discharge for a median of 5.6 years. Of 678 patients originally in the cohort, 660 (98% male) were included in the analysis (mean age 74±6 years). During the study, 314 subjects (48%) died and a U-shaped association between weight change and mortality was observed. Those who were relatively weight stable had the lowest mortality; compared with this group, the adjusted relative risk of death for those who lost 1-3kg per year was 2.14 (95% CI: 1.52-3.00) and for those who lost more than 3kg per year was 3.59 (95% CI: 2.58-4.99). The adjusted relative risk of death for those who gained 1-3kg per year was 1.38 (95% CI: 0.91-2.10) and for those who gained more than 3kg per year was 3.73 (95% CI: 2.34-5.94).

Takata Y et al, 2007 (positive quality) analyzed data from a cohort study conducted in a community-based setting in Japan to evaluate association between BMI and all-cause mortality and cardiovascular disease (CVD) in an 80-year-old population (Initial N=1,282; Final N=697; 54.4%; 277 men and 420 women) with a four-year follow up. Subjects underwent physical and laboratory blood examinations. The hazard ratios for all-cause mortality were lower in overweight subjects (BMI>25.0kg/m²) than in underweight (BMI<18.5kg/m²) or normal-weight (BMI 18.5-24.9kg/m²) subjects. The hazard ratios for mortality due to CVD in overweight subjects were 78% less (HR=0.22, 95% CI=0.06-0.77) than those in underweight subjects and those in normal weight subjects were 78% less (HR=0.22, 95% CI=0.08-0.60) than those in underweight subjects. Mortality due to CVD was 4.6 times (HR 4.64, 95% CI=1.68-12.80) as high in underweight subjects as in normal-weight subjects. Mortality due to cancers was 88% lower (HR=0.12, 95% CI=0.02-0.78) in the overweight group than in the underweight group. There were no differences in mortality due to pneumonia. Authors concluded that overweight status was associated with longevity and underweight with short life, due to lower and higher mortality, respectively, from CVD and cancer.

Vischer UM et al, 2009 (neutral quality) analyzed data from a prospective cohort study conducted in France to determine the impact of cardiometabolic risk factors on mortality in elderly subjects hospitalized in geriatric wards. Anthropometric measurements and blood testing were completed at baseline between May 2000 to November 2001, and participants were followed up until either death or the last medical contact

through April 2004. A total of 331 subjects were included in the analysis (86 men, 245 women, mean age 85 ± 7 years). Two-year total mortality was predicted by age, diabetes, low BMI, low diastolic BP, low total cholesterol and HDL cholesterol (HDL-C) and previous cardiovascular events, and in multivariate analyses, the strongest mortality predictors were low BMI, low HDL-C and previous myocardial infarction.

Volpato S et al, 2004 (positive quality) analyzed data from a prospective cohort study conducted in Italy to examine the relationship between BMI, body composition, and four-year all-cause mortality in older nursing home residents. Anthropometric, nutritional and metabolic measurements were obtained at baseline, and all-cause mortality was determined using nursing home medical records or follow-up interviews with proxies for residents who had moved. Of 410 nursing home residents, 344 were included in the analysis (272 females, 72 males, mean age 82.2 years). During the four-year follow-up period, 179 residents died. In fully adjusted models, there was no association between BMI levels and risk of mortality; subjects in the top tertile had the same likelihood of mortality as those in the lowest tertile (RR=0.94, 95% CI: 0.61-1.43). However, there was a strong and significant inverse association between body cell mass levels and mortality (relative risk for the highest tertile=0.55, 95% CI: 0.35-0.87, $P < 0.01$) and participants with high body cell mass had comparable survival rates across all BMI tertiles.

Weiss A et al, 2008 (positive quality) conducted a retrospective cohort study in Israel to examine the long-term effects of overweight on mortality in older adults. During a two-year period from 1999-2000, subjects >60 years old were enrolled in the study, and height and weight data was collected from their medical records and used to calculate BMI. Subjects were followed for an average of 3.5 years until 2004, with mortality data being collected from death certificates. The final sample included 470 adults (226 men, 244 women; mean age=82 years). During the 3.5 year follow-up period, 248 subjects died. Patients with the lowest BMI ($<22 \text{ kg/m}^2$) had the highest rate of mortality, with the age-adjusted mortality rate decreasing from 24/100 patient-years in the lowest BMI quartile to 9.6/100 patient-years in the highest BMI quartile ($>28 \text{ kg/m}^2$; $P < 0.001$). The highest quartile of BMI decreased all-cause mortality by a relative 33% (95% CI 13%, 49%). The authors concluded that in older adults, higher BMI was associated with reduced mortality risk.

Woo J et al, 2001 (neutral quality) conducted a prospective cohort study in Hong Kong (China) to determine the relationship between longitudinal changes in anthropometric measures and mortality, morbidity, functional capacity, physical performance measurement, self-perceived health and psychosocial measures. Subjects were assessed at baseline and followed up after 36 months. Measures included height, weight, BMI, body composition, mortality and self-reported morbidity. The final sample included 1,171 subjects after 36 months, and all subjects were >70 years of age at baseline. After 36 months, 18.8% of men and 20.9% of women lost ≥ 5 kg. All anthropometric measures, except triceps skin-fold in men, decreased regardless of presence or absence of disease. Women had greater decreases in arm circumference, triceps skin-fold thickness and total body fat compared to men, while men had a greater decrease in fat-free mass. Lower anthropometric measures were associated with greater mortality and morbidity, and decreases in fat-free mass and total body fat were associated with worse outcomes, especially in women. Waist-to-hip ratio was not associated with morbidity or mortality. The authors concluded that even in the absence of disease, older adults experience loss of weight, which in turn is associated with increased morbidity and mortality.

Yaari S and Goldbourt U, 1998 (positive quality) analyzed prospective cohort data from Israel to determine the association between weight change and mortality. Subjects were men from the Israeli Ischemic Heart Disease Study who were assessed at baseline (40-65 years) in 1963, re-assessed in 1968, and followed for 18 years. Height and weight were measured at baseline and five years later and mortality follow-up was via the Israeli Mortality Registry. The final sample included 9,228 men. Men who lost 5kg or more between 1963 and 1968 ("extreme weight losers") had higher mortality risk compared to the weight stable group for total mortality (1.36, 95% CI 1.20-1.55), cardiovascular mortality (1.40, 95% CI 1.16-1.69), non-cardiovascular mortality (1.33, 95% CI 1.11-1.59), coronary heart disease mortality (1.55, 95% CI 1.25-19.3), and cancer mortality (0.90, 95% CI 0.65-1.24). These risks decreased by one-third after adjustment for coronary heart disease risk factors and morbidity. Weight loss was also associated with diabetes mellitus and decrease serum total cholesterol levels. The authors conclude that both voluntary and involuntary weight loss might be

associated with a small increase in risk from all-cause mortality.

Longitudinal Observational Studies (2)

Locher JL et al, 2007 (positive quality), a longitudinal observational study conducted in the United States, evaluated the association between body mass index, recent intentional or unintentional weight loss, and mortality in older adults participating in the University of Alabama at Birmingham Study of Aging. Participants were given a baseline questionnaire regarding mobility and overall health status; weight and height measurements were taken. Telephone interviews were conducted every six months for three years and mortality was validated through the Social Security Death Index. Of 1,000 participants recruited, 983 were included in the analysis (496 male, 487 female, mean age 75.30 years). Unintentional weight loss and underweight BMI were associated with elevated three-year mortality rates, however, there was no association with being overweight or obese on mortality, nor was there an association with intentional weight loss and mortality.




Woo J et al, 2002 (neutral quality), a longitudinal observational study of 36 months conducted in China examined effect of age on the relationship between BMI and waist circumference (WC) and the effectiveness of BMI, WC and waist-to-hip ratio (WHR) in predicting mortality and cardiovascular risk in older adults. A random sample of 2,032 Chinese subjects (990 male, 1,033 female) with a mean age of 80.1±7.5 years were interviewed and examined at baseline and after 36 months. Final N=1,690 at 36-month follow-up. Subjects completed a medical history questionnaire and had their height, weight, waist, hip and blood pressure measured. Results show that WC values corresponding to BMI values of 25 and 30kg/m² were higher in elderly (92 for men; 88 for women) compared with younger subjects (85 for men; 78 for women). BMI and WC are inversely associated with mortality, in both men and women, positively associated with diabetes in men but not in women. Waist circumference was positively associated with hypertension in men and women. Waist-to-hip ratio was not associated with any outcome measures.



Structural Equation Model (1)



Yang Z et al, 2008 (positive quality), a structural equation model study conducted in the United States, constructed a system of simultaneous equations to quantify the relationship between annual changes in BMI, experience of chronic conditions, changes in functional status, and mortality using data from the Cost and Use files of the Medicare Current Beneficiary Survey (MCBS), which included at least two years of observational data per individual between the years of 1992-2001. A total of 28,966 individuals aged 65 and older were included in the analysis, resulting in an analytical sample of 85,038 person-year observations. The elderly with normal weight at age 65 years experience higher life expectancy and lower disability rates than the same age cohorts in other weight categories. The relationship between BMI and poor health outcomes was found to be non-linear, with either high or low BMI being associated with poor health outcomes. The results of the study suggest that optimal BMI at age 65 appears to be within the normal weight spectrum of 18.5-24.9kg/m².




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Author, Year, Study Design, Class, Rating	Study Name	Population	Methodology	Outcomes
Allison DB et al .1997 Study Design: Prospective Longitudinal	Longitudinal Study of Aging.	N=7,397 (>70 years of age). Location: United States.	BMI was based on self-reported height and weight, while mortality was obtained by record matching to the	The relationship between BMI and mortality was U-shaped for both men and women; the minimum mortality occurred at a BMI of 31.7kg/m ² for women and



<p>Cohort Study</p> <p>Class: B</p> <p>Rating: </p>			<p>National Death Index.</p> <p>Baseline occurred in 1984, and subjects were followed through 1990.</p>	<p>28.8kg/m² for men.</p>
<p>Amador LF et al 2006</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>Established Population for the Epidemiological Study of the Elderly (ESPESE).</p>	<p>N=1,749 (>65 years at baseline).</p> <p>Location: United States.</p>	<p>Weight Δ was based on measurements made at baseline and at the two-year follow-up, and participants were followed for mortality over the next five years.</p>	<p>After controlling for confounding variables, compared to the weight stable group, the HR of death for the group that lost $\geq 5\%$ of their weight was 1.32 (95% CI: 1.04-1.67) and for the group that gained $\geq 5\%$ of their weight was 0.77 (95% CI: 0.57-1.04).</p>
<p>Arnold AM, Newman AB et al, 2010</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>Cardiovascular Health Study.</p>	<p>N=3,278 adults (39% men; mean age=80 years).</p> <p>Location: United States.</p>	<p>Weight was measured annually in a clinic between 1992 and 1999. Subjects were then followed until 2006 with regular assessments of activities of daily living, mobility and mortality.</p>	<p>Weight loss was associated with \uparrow mortality (1.58 (95% CI 1.33, 1.88), as was weight cycling (1.66 (95% CI 1.38, 2.00).</p>
<p>Corrada MM et al 2006</p> <p>Study Design: Population-based Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>Leisure World Cohort Study.</p>	<p>N=13,451 residents (mean age 73 years).</p> <p>Location: United States.</p>	<p>All 13,978 residents of the Leisure World Laguna Hills retirement community returned mailed questionnaires in 1981, 1982, 1983 and 1985. Residents reported weight and height at age 21, and weight Δ was calculated as percent Δ in weight from age 21 to</p>	<p>Relative to normal weight, being underweight (RR=1.51, 95% CI: 1.38-1.65) or obese (RR=1.25, 95% CI: 1.13-1.38) at study entry was associated with \uparrow mortality.</p> <p>In addition, residents who were either overweight or obese at age 21 also had \uparrow mortality (RR=1.17, 95% CI: 1.09-1.25); obesity was significantly associated with \uparrow mortality only among persons under age 75 years</p>


			study entry. All-cause mortality was confirmed by periodic resurveys, reviews of local hospital discharge records, and determination of vital status through searches of national and commercial death indexes.	and among never or past smokers.
de Groot CP et al. 2002 Study Design: Prospective Cohort Study Class: B Rating: 	SENECA study.	N=662 subjects (292 men and 370 women). Location: Europe.	Baseline measurements were taken in 1988/1989 and repeated in 1993 and 1999.	Weight loss during the first four years of follow-up was associated with ↑ mortality rates in men (crude RR=2.2, P<0.0001).
Dey DK et al 2001 Study Design: Longitudinal Cohort Study Class: B Rating: 		N=2,593 (aged 70 years and older). Location: Sweden.	Three birth cohorts (born in 1901/1902, 1906/1907 and 1911/1912) were followed over a 15-year period and BMI was based on measured height and weight.	The RR for 15-year mortality were highest in the lowest BMI quintiles of males (RR=1.20, 95% CI: 0.96-1.51) and females (RR=1.49, 95% CI: 1.14-1.96). After exclusion of the first five years of death, no excess risks were found in males for following five-year and 10-year mortality across the quintiles, but in females, a U-shaped relation was observed. BMI ranges with lowest 15-year mortality were 27-29kg/m ² in non-smoking males and 25-27kg/m ² in non-smoking females. In addition, a weight loss of >10% between ages 70 and 75 resulted in a significantly

				<p>↑ risk for subsequent five-year and 10-year mortality in both sexes relative to those with stable weights.</p>
<p>Diehr P et al 2008</p> <p>Study Design: Longitudinal Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>Cardiovascular Health Study.</p>	<p>N=5,888 (mean age 75.7 years).</p> <p>Location: United States.</p>	<p>Based on multistate life tables, the age- and sex-specific probabilities of transition from one health state to another and from one weight category to another were estimated.</p> <p>Height and weight were measured and mortality was assessed at follow-up.</p>	<p>Women who were healthy and at normal weight at age 65 years have a life expectancy of 22.1 years, with 9.6 of those years as overweight and obese and 5.3 of those years in fair or poor health.</p> <p>For both men and women, being underweight at age 65 years was associated with worse outcomes than being normal weight.</p> <p>Being overweight or obese was rarely associated with worse outcomes than being normal weight and was sometimes associated with significantly better outcomes.</p>
<p>Diehr P, Bild DE et al, 1998</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>Cardiovascular Health Study.</p>	<p>N=4,317 adults (2,410 women, 1,907 men; mean age=73 years).</p> <p>Location: United States.</p>	<p>Body mass index (BMI) was determined at baseline using measured height and weight and follow-up all cause mortality was determined five years later.</p>	<p>There was an inverse association between BMI and mortality, such that those who weighed the least had the highest mortality rates ($P<0.01$).</p> <p>Subjects who lost $\geq 10\%$ of their weight since age 50 had a higher mortality rate (16% for women, 30% for men); however, when this group was excluded from analyses, there was no longer a relationship between BMI and mortality.</p>




<p>Dolan CM, Kraemer H et al, 2007</p> <p>Study Design: Cohort study</p> <p>Class: B</p> <p>Rating: </p>	<p>Study of Osteoporotic Fractures.</p>	<p>N=8,029 women (mean age=72 years).</p> <p>Location: United States.</p>	<p>At baseline, body composition was measured via bioelectrical impedance and BMI was determined using measured height and weight. Average follow-up occurred eight years later, when mortality was assessed.</p>	<p>Mortality rates were lowest for women in the middle distribution of each measure of body size. Lowest mortality rates were seen in the BMI range from 24.6 to 29.8kg/m², and all body measures had a U-shaped relation with mortality (P<0.05), such that ↑ mortality was associated with BMI above and below this range.</p>
<p>Ellekjaer H, Holmen J et al, 2001</p> <p>Study Design: Prospective cohort</p> <p>Class: B</p> <p>Rating: </p>		<p>N=3,121 men and N=3,271 women (>70 years and older).</p> <p>Location: Norway.</p>	<p>Height, weight and BMI were determined at baseline.</p> <p>Cerebrovascular and cardiovascular mortality were assessed at a mean follow-up time of 7.7 years.</p>	<p>In women, a negative association between BMI and mortality from CVD death was found after age-adjustments (P=0.03).</p> <p>There was no association between BMI and mortality from CHD in men.</p> <p>A negative association was found between increasing BMI and all-cause mortality in men and women in age-adjusted analyses (both P<0.01), but in multivariate analyses, the negative association was statistically significant only in women (P<0.01).</p>
<p>Grabowski DC and Ellis JE 2001</p> <p>Study Design: Retrospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>Longitudinal Study of Aging.</p>	<p>N=7,459 (62% female, 38% male, mean age 76.8 years).</p> <p>Location: United States.</p>	<p>Baseline information, including self-reported height and weight, was collected in 1984 and survival was measured for eight years until December 1991 using the National Death Index.</p>	<p>Adjustment for confounding variables demonstrated ↓ mortality in obese older people (HR=0.86, 95% CI: 0.77-0.97) compared with normal-weight older people.</p> <p>In addition, after adjustment, underweight older people remained more likely to die (HR=1.46, 95% CI: 1.30-1.64) than normal-weight older people.</p>




<p>Graham JE, Snih SA et al, 2009</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>		<p>N=1,996 Mexican American older adults (42% men; mean age=75 years; mean BMI=28kg/m²).</p> <p>Location: United States.</p>	<p>The study dataset covers the period from wave two (1995-1996) through wave five (1993-1994). Data were collected from in-person interviews and performance evaluations at each wave.</p> <p>Frailty was determined using a five-item scale based on weight loss, exhaustion, walking speed, grip strength, physical activity.</p>	<p>In the fully adjusted model, the pre-frail group had 1.25 times (95% CI: 1.07, 1.46) the odds of mortality relative to the non-frail group, and the group classified as frail at baseline had an ↑ odds of 1.81 (95% CI: 1.41, 2.31) of mortality.</p>
<p>Inoue K et al 2006</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>		<p>N=371 (>65 years at baseline).</p> <p>Location: Japan.</p>	<p>BMI was calculated from measured height and weight, and the mortality register was followed for five years.</p>	<p>The mortality rate in the low BMI group was approximately twice that in the normal BMI group, and no deaths were observed in the high BMI group. In multivariate analyses, age and low BMI were associated with mortality.</p>
<p>Janssen I, 2007</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>Cardiovascular Health Study.</p>	<p>N=4,96 (44.6% men: 43% 65-70 years, 33% 71-76 years, 18% 77-82 years, and 7% >83 years).</p> <p>Location: United States.</p>	<p>Weight and height were measured at baseline. Mortality and MI or stroke were ascertained for up to nine years, diabetes status was measured at baseline, three-year, and seven-year follow-up examinations, and cancer status was measured at baseline, one-year,</p>	<p>In the final adjusted model, the risk estimates for all-cause mortality were 11% lower in the overweight group and 17% lower in the obese group compared to the normal weight group (P<0.05). Compared with the normal weight group, the HR for MI, stroke and cancer were not different in the overweight group (P>0.05). The risk for developing diabetes was increased by 78% within the overweight group (vs.</p>



			three-year and four-year follow-up examinations.	normal weight group, $P<0.01$).
<p>Janssen I, Katzmarzyk PT and Ross R 2005</p> <p>Study Design: Longitudinal Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	Cardiovascular Health Study.	<p>N=5,200 (>65 years; 2,263 males and 2,937 females).</p> <p>Location: United States.</p>	<p>The baseline exam was conducted between June 1989 and June 1990, and BMI was calculated based on measured height and weight; waist circumference (WC) was also measured. The cohort was followed annually for nine years after the baseline exam, and all-cause mortality was assessed through reviews of obituaries, medical records, death certificates and the US Center for Medicare and Medicaid Services health utilization database for hospital stays.</p>	<p>When examined individually, BMI and WC were both negative predictors of mortality, however, when examined simultaneously, BMI was a negative predictor and WC was a positive predictor.</p> <p>After controlling for WC, mortality risk ↓ 21% for every SD ↑ in BMI and after controlling for BMI, mortality risk ↑ 13% for every SD ↑ in WC.</p>
<p>Kalmijn S et al 1999</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	Honolulu Heart Program.	<p>N=3,594 (aged 71-93 years).</p> <p>Location: United States.</p>	<p>Body weight, height, body composition and WHR ratio were measured during the study period; data were extracted from the 1991-1993 follow-up visits and included 4.5 years of follow-up.</p>	<p>Higher BMI was associated with ↓ adjusted mortality risks (RR for the highest vs. lowest quintile-based category=0.5, 95% CI=0.4-0.6, P for trend <0.001).</p> <p>The relationship between WHR and mortality appeared to be U-shaped, but after adjustment for BMI, a higher WHR steadily ↑ the risk of dying (RR for the highest vs. lowest category=1.5, 95% CI:</p>



				1.1-2.0, P for trend=0.004).
<p>Keller HH and Ostbye T, 2005</p> <p>Study Design: Cohort study</p> <p>Class: B</p> <p>Rating: </p>	<p>Canadian Study of Health and Aging.</p>	<p>N=539 (30.6% were aged 65-74 years, 55.8% were aged 75-84 years, and 13.5% were aged 85 years or older).</p> <p>Location: Canada.</p>	<p>Participants underwent a clinical examination (including body weight measurements) in 1991 and 1996, and mortality was determined via decedent questionnaires and death certificate information.</p>	<p>A significant ↓ in BMI predicted death (OR, 2.10; 95% CI: 1.17, 3.80); other factors predictive of death were age and cognitive impairment.</p>
<p>Knudtson MD, Klein BE et al, 2005</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>		<p>N=4,926.</p> <p>Location: United States.</p>	<p>Subjects were recruited in 1988 and 1990 and followed for more than 10 years. A medical examination and questionnaire were administered at baseline. Death was determined via follow-up telephone calls and review of vital statistics records.</p>	<p>After controlling for age, medical and lifestyle factors, both men and women had ↑ mortality rates over >10-year period for increasing categories of weight loss (HR 1.16, 95% CI 1.06, 1.27 for men; HR 1.23, 95% CI 1.13, 1.34 for women).</p>
<p>Kulminski AM et al 2008</p> <p>Study Design: Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>National Long-Term Care Survey.</p>	<p>N=4,791 (>65 years at baseline).</p> <p>Location: United States.</p>	<p>BMI were based on self-reported height and weight; mortality was followed for nine years based on Medicare vital statistics files.</p>	<p>The RR of death as a function of BMI formed a non-symmetric U-shaped pattern, with larger risks associated with lower BMI (<22.0kg/m²) and minimal risks for BMI 25.0-34.9kg/m². Non-disabled individuals exhibited a similar U-shaped pattern, but with lower risks associated with lower BMI. For disabled individuals, the mortality-risk pattern was higher for lower BMI</p>

				(<22.0kg/m ²) and flat for higher BMI, thus exhibiting an inverse J shape.
<p>Locher JL et al 2007</p> <p>Study Design: Longitudinal Observational Study</p> <p>Class: B</p> <p>Rating: </p>	<p>University of Alabama at Birmingham Study of Aging.</p>	<p>N=983 (496 male, 487 female, mean age 75.30 years).</p> <p>Location: United States.</p>	<p>Participants were given a baseline questionnaire regarding mobility and overall health status; weight and height measurements were taken. Telephone interviews were conducted every six months for three years and mortality was validated through the Social Security Death Index.</p>	<p>Unintentional weight loss and underweight BMI were associated with ↑ three-year mortality rates, however, there was no association with being overweight or obese on mortality, nor was there an association with intentional weight loss and mortality.</p>
<p>Mazza A et al 2007</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>Cardiovascular Study in the Elderly (CASTEL).</p>	<p>N=3,292 (1,281 males and 2,001 females, mean age 73.8±5.3 years at baseline).</p> <p>Location: Italy.</p>	<p>BMI was calculated based on measured height and weight from the initial screening, and participants received an annual follow-up for mortality for 12 years, which was determined from the Registry office and double-checked for causes of death by referring to hospitals, retirement homes or physicians' files.</p>	<p>BMI inversely predicted overall and cancer mortality in men only, and there was no relationship between BMI and coronary or cerebrovascular mortality.</p> <p>The relationship between BMI and mortality remained significant only in men aged ≤76 years; overall mortality was 64.7% in the first BMI quintile, 54.9% in the second BMI quintile, 54.1% in the third BMI quintile, 53.3% in the fourth BMI quintile and 52.5% in the last BMI quintile.</p>
<p>Newman AB et al 2001</p> <p>Study Design: Longitudinal Observational</p>	<p>Cardiovascular Health Study.</p>	<p>N=4,714 (>65 years at baseline).</p> <p>Location: United States.</p>	<p>Weight was measured at baseline and at the three-year follow-up visit, and participants were</p>	<p>While weight gain was not associated with ↑ risk of mortality, weight loss of 5% or more was associated with an ↑ risk of mortality that persisted after multivariate</p>



<p>Cohort Study</p> <p>Class: B</p> <p>Rating: </p>			<p>followed for four years for mortality.</p>	<p>adjustment (HR=1.67, 95% CI: 1.29-2.15).</p> <p>Those with weight loss and with low baseline weight had the highest crude mortality rate, although the HR for weight loss was similar for all tertiles of baseline weight compared with those whose weight was stable.</p>
<p>Nguyen ND et al 2007</p> <p>Study Design: Longitudinal Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>Dubbo Osteoporosis Epidemiology Study.</p>	<p>N=1,703 (1,059 women and 644 men, aged 60 and older).</p> <p>Location: Australia.</p>	<p>Bone density was measured by DEXA at baseline and approximately every two years afterward, while all-cause mortality was recorded annually between 1989 and 2004.</p>	<p>In men, independent risk factors of all-cause mortality included a rate of bone density loss of at least 1% per year, a rate of weight loss of at least 1% per year and a weight fluctuation of at least 3%.</p> <p>In women, lower baseline bone density was also an independent risk factor of mortality in addition to the factors observed in men.</p> <p>However, in both sexes, baseline weight was not an independent and significant predictor of mortality risk.</p>
<p>Payette H et al 1999</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>		<p>N=288 (207 women, 81 men, mean age 78.2±7.6 years).</p> <p>Location: Canada.</p>	<p>Height, weight and dietary intake were measured at baseline, and subjects were followed for mortality for three to five years.</p>	<p>During the follow-up period, 102 participants (35.4%) died; predictors included age, sex, BMI, weight loss and functional status.</p> <p>In multivariate analyses, weight loss at baseline was a significant predictor of mortality (RR=1.76, 95% CI: 1.15-2.71), as was male gender (RR=2.71, 95% CI: 1.73-4.24) and age at baseline (RR=1.40, 95% CI: 1.06-1.86).</p>



<p>Price GM, Uauy R et al, 2006</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>		<p>N=14,833 (5,715 men, 9,118 women).</p> <p>Location: United Kingdom.</p>	<p>Subjects had anthropometric measures taken at a clinic visit and average follow-up time was 5.9 years.</p>	<p>Compared to the lowest BMI quintile ($<23\text{kg/m}^2$ in men, $<22.3\text{kg/m}^2$ in women), adjusted HRs for mortality were less than one for all other BMI quintiles (P=0.0003 for men, P=0.0001 for women).</p> <p>↑ WHR was associated with ↑ HRs in men (P=0.008) and women (P=0.0002).</p> <p>In men, BMI was not associated with circulatory mortality, but it was positively associated in women (P=0.004).</p>
<p>Reynolds MW et al 1999</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>		<p>N=648 were included in the analysis (mean age 73 ± 6.1 years).</p> <p>Location: United States.</p>	<p>Three home interviews were conducted annually from 1984 to 1986; height and demographic information was obtained during the baseline interview, while weight was measured at each interview.</p>	<p>During the follow-up period, 106 women (16%) died; women with low baseline BMI ($<23\text{kg/m}^2$), regardless of weight change, and those who lost weight, regardless of baseline BMI, had ↑ mortality risk. In addition, women with average baseline BMI ($23\text{--}28\text{kg/m}^2$) and weight loss had a very high mortality risk (HR=3.84, 95% CI: 2.14-6.89). Women who weight cycled had ↑ mortality risk at both low and high baseline weights.</p>
<p>Rodriguez C, Calle EE et al, 2002</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>		<p>N=300,537 post-menopausal women.</p> <p>Location: United States.</p>	<p>BMI at baseline was calculated based on self-reported height and weight, and subjects were followed for 16 years, when mortality was determined using personal inquiries and the National</p>	<p>Ovarian cancer mortality rates were ↑ in overweight (1.16 (95% CI 1.04, 1.30) and obese (1.26 (95% CI 1.07, 1.48) women compared to normal weight women. This relationship was mediated by use of postmenopausal estrogens, as the ↑ risk of ovarian cancer among obese women was limited to those who</p>

			Death Index.	never used postmenopausal estrogen (1.36 (95% CI 1.12, 1.66)).
<p>Shea MK, Houston DK et al, 2010</p> <p>Study Design: Randomized Controlled Trial</p> <p>Class: A</p> <p>Rating: </p>		<p>N=319 adults (72% female; mean age=96 years; mean BMI=34kg/m²).</p> <p>Location: United States.</p>	<p>Subjects were randomized to one of four treatment groups: Dietary weight loss, exercise, dietary weight loss + exercise, or a healthy lifestyle control group. The intervention was 18 months long. Body weight and height were measured and used to determine BMI and weight status, and mortality was determined using the Social Security Index and the National Death Index.</p>	<p>The mortality rate for those randomized to the 18-month weight loss intervention (mean weight loss=-4.8kg) was lower than that for those not randomized to the weight loss intervention (mean weight loss= -1.4kg) (HR 0.5, 95% CI 0.3-1.0). Results did not Δ when adjusted for age, gender, baseline weight status or magnitude of weight loss.</p>
<p>Sorsensen TIA, Rissanen A et al, 2005</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	The Finnish Twin Cohort.	<p>N=2,957 (BMI>25kg/m²; 268 died during the follow-up period).</p> <p>Location: Finland.</p>	<p>Subjects were recruited in 1975 and followed through 1999. Weight and BMI was determined using self-reported height and weight and mortality as determined using the Statistics Finland database.</p>	<p>Compared with the group not intending to lose and able to maintain stable weight, the HRs in the group intending to lose weight were 0.84 (95% CI 0.49-1.48) for those with stable weight, 1.86 (95% CI 1.22-2.87) for those losing weight and 0.93 (95% CI 0.55-1.56) for those gaining weight.</p> <p>In the group not intending to lose weight, HRs were 1.1 (95% CI 0.82-1.66) for those who did not lose weight and 1.57 (95% CI 1.08-2.30) for those gaining weight.</p>

<p>Sullivan DH et al 2004</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>Geriatric Anorexia Nutrition (GAIN) registry.</p>	<p>N= 894 (mean age, 86±8 years) in 96 long-term care facilities distributed among eight states.</p> <p>Location: United States.</p>	<p>Nutritional, health status and demographic data was obtained through nursing home charts or other means. Each subject was followed for six months.</p>	<p>Predictors of a $\geq 5\%$ weight gain within six months included BMI (adjusted OR, 0.89; 95% CI, 0.85 to 0.93), age (adjusted OR, 0.96; 95% CI, 0.94-0.98), feeding dependency (adjusted OR, 0.55; 95% CI, 0.34 to 0.89) and receiving appetite stimulants (adjusted OR, 1.70; 95% CI, 1.06 to 2.72). A weight loss during the six-month period was associated with nearly two-fold \uparrow in the risk of death (adjusted RR: 1.95, 95% CI, 1.46 to 2.66).</p>
<p>Sullivan DH, Morley JE et al, 2002</p> <p>Study Design: Prospective cohort study</p> <p>Class: B</p> <p>Rating: </p>		<p>N=660 (98% male; mean age 74±6 years).</p> <p>Location: United States.</p>	<p>Data evaluated the prognostic significance of weight Δ in frail elderly patients in a Department of Veterans Affairs hospital.</p> <p>At admission and discharge, subjects completed a standardized diagnostic evaluation, and weights were recorded before admission, during the current hospitalization and after discharge for a median of 5.6 years.</p>	<p>A U-shaped association between weight Δ and mortality was observed.</p> <p>Those who were relatively weight stable had the lowest mortality; compared with this group, the adjusted RR of death for those who lost 1-3kg per year was 2.14 (95% CI: 1.52-3.00) and for those who lost >3kg per year was 3.59 (95% CI: 2.58-4.99).</p> <p>The adjusted RR of death for those who gained 1-3kg per year was 1.38 (95% CI: 0.91-2.10) and for those who gained >3kg per year was 3.73 (95% CI: 2.34-5.94).</p>
<p>Takata Y et al 2007</p> <p>Study Design: Cohort Study</p> <p>Class: B</p>		<p>N=697 (277 men and 420 women; age 80 years at baseline).</p> <p>Location: Japan.</p>	<p>Data were collected in community-based setting in Japan to evaluate association between BMI and all-cause mortality and CVD in a</p>	<p>The HRs for mortality due to CVD in overweight subjects were 78% less (HR=0.22, 95% CI=0.06-0.77) than those in underweight subjects, and those in normal weight subjects were 78% less (HR=0.22, 95%</p>

<p>Rating: </p>			<p>four-year follow up. Subjects underwent physical and laboratory blood examinations.</p>	<p>CI=0.08-0.60) than those in underweight subjects.</p> <p>Mortality due to CVD was 4.6 times (HR 4.64, 95% CI=1.68-12.80) as high in underweight subjects as in normal-weight subjects.</p> <p>Mortality due to cancers was 88% lower (HR=0.12, 95% CI=0.02-0.78) in the overweight group than in the underweight group.</p>
<p>Vischer UM et al 2009</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>		<p>N=331 (86 men, 245 women, mean age 85±7 years).</p> <p>Location: France.</p>	<p>Anthropometric measurements and blood testing were completed at baseline between May 2000 to November 2001, and participants were followed up until either death or the last medical contact through April 2004.</p>	<p>Two-year total mortality was predicted by age, diabetes, low BMI, low DBP, low TC and HDL-C, and previous cardiovascular events. In multivariate analyses, the strongest mortality predictors were low BMI, low HDL-C and previous MI.</p>
<p>Volpato S et al 2004</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>		<p>N=344 (272 females, 72 males, mean age 82.2 years).</p> <p>Location: Italy.</p>	<p>Anthropometric, nutritional and metabolic measurements were obtained at baseline, and all-cause mortality was determined at a four-year follow-up using nursing home medical records or follow-up interviews with proxies for residents who had moved.</p>	<p>In fully adjusted models, there was no association between BMI levels and risk of mortality; subjects in the top tertile had the same likelihood of mortality as those in the lowest tertile (RR=0.94, 95% CI: 0.61-1.43).</p> <p>However, there was a strong and significant inverse association between body cell mass levels and mortality (RR for the highest tertile=0.55, 95% CI: 0.35-0.87, P<0.01), and participants with high body cell mass had comparable survival rates across all BMI tertiles.</p>




<p>Weiss A, Beloosesky Y et al, 2008</p> <p>Study Design: Retrospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>		<p>N=470 (226 men, 244 women; mean age=82 years).</p> <p>Location: Israel.</p>	<p>During a two-year period from 1999-2000, subjects >60 years old were enrolled in the study, and height and weight data was collected from their medical records and used to calculate BMI. Subjects were followed for an average of 3.5 years until 2004, with mortality data being collected from death certificates.</p>	<p>Patients with the lowest BMI (<22kg/m²) had the highest rate of mortality, with the age-adjusted mortality rate decreasing from 24/100 patient-years in the lowest BMI quartile to 9.6/100 patient-years in the highest BMI quartile (>28kg/m²; P<0.001).</p> <p>The highest quartile of BMI ↓ all-cause mortality by a relative 33% (95% CI 13%, 49%).</p>
<p>Woo J, Ho SC et al, 2002</p> <p>Study Design: Longitudinal, observational study</p> <p>Class: B</p> <p>Rating: </p>		<p>N=2,032 Chinese subjects (990 male, 1,033 female) with a mean age of 80.1±7.5 years were interviewed and examined at baseline and after 36 months.</p> <p>Final N=1,690 at 36-month follow-up.</p> <p>Location: China.</p>	<p>A random sample of Subjects completed a medical history questionnaire and had their height, weight, waist, hip and BP measured.</p>	<p>BMI and WC are inversely associated with mortality, in both men and women, positively associated with diabetes in men but not in women.</p> <p>WC was positively associated with HTN in men and women.</p> <p>WHR was not associated with any outcome measures.</p>
<p>Woo, Ho et al 2001</p> <p>Study Design: Prospective cohort study</p> <p>Class: B</p> <p>Rating: </p>		<p>N=1,171 (>70 years of age at baseline).</p> <p>Location: Hong Kong.</p>	<p>Subjects were assessed at baseline and followed up after 36 months. Measures included height, weight, BMI, body composition, mortality and self-reported morbidity.</p>	<p>Lower anthropometric measures were associated with greater mortality and morbidity and ↓ in fat-free mass and total body fat were associated with worse outcomes, especially in women.</p>

<p>Yaari S and Golbourn U, 1998</p> <p>Study Design: Prospective Cohort Study</p> <p>Class: B</p> <p>Rating: </p>	<p>Israeli Ischemic Heart Disease Study.</p>	<p>N=9,228 men.</p> <p>Location: Israel.</p>	<p>Subjects were assessed at baseline (40-65 years) in 1963, re-assessed in 1968 and followed for 18 years. Height and weight were measured at baseline and five years later and mortality follow-up was via the Israeli Mortality Registry.</p>	<p>Men who lost ≥ 5kg between 1963 and 1968 (“extreme weight losers”) had higher mortality risk compared to the weight stable group for total mortality (1.36, 95% CI 1.20-1.55), cardiovascular mortality (1.40, 95% CI 1.16-1.69), non-cardiovascular mortality (1.33, 95% CI 1.11-1.59), CHD mortality (1.55, 95% CI 1.25-19.3) and cancer mortality (0.90, 95% CI 0.65-1.24). These risks ↓ by one-third after adjustment for CHD risk factors and morbidity.</p> <p>Weight loss was also associated with diabetes mellitus and decrease serum total cholesterol levels.</p>
<p>Yang Z, Bishai D and Harman J 2008</p> <p>Study Design: Longitudinal Study</p> <p>Class: B</p> <p>Rating: </p>	<p>Structural equation model.</p>	<p>N=28,966 individuals aged 65 and older were included in the analysis, resulting in an analytical sample of 85,038 person-year observations.</p> <p>Location: United States.</p>	<p>Constructed a system of simultaneous equations to quantify the relationship between annual Δs in BMI, experience of chronic conditions, changes in functional status, and mortality using data from the Cost and Use files of the Medicare Current Beneficiary Survey (MCBS), which included at least two years of observational data per individual between the years of 1992-2001.</p>	<p>The elderly with normal weight at age 65 years experience ↑ life expectancy and ↓ disability rates than the same age cohorts in other weight categories.</p> <p>The relationship between BMI and poor health outcomes was found to be nonlinear, with either ↑ or ↓ BMI being associated with poor health outcomes.</p> <p>The results of the study suggest that optimal BMI at age 65 appears to be within the normal weight spectrum of 18.5-25kg/m².</p>

Research Design and Implementation Rating Summary


For a summary of the Research Design and Implementation Rating results, [click here](#).

Worksheets


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